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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/479,862 | 01/10/2000 | TAKANORI OKURA | OKURA-1A | 3626 |

1444 7590 05/23/2002

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| EXAMINER |
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SHUKLA, RAM R

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| ART UNIT | PAPER NUMBER |
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1632

DATE MAILED: 05/23/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/479,862

Applicant(s)

OKURA ET AL.

Examiner

Ram Shukla

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3-8, 15 and 17-20 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 3, 15 and 17-20 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *detailed action*.

DETAILED ACTION

1. Applicant's response and amendment filed 2-21-02 have been entered.
2. Claims 1, 2, 9-14, and 16 have been cancelled.
3. It is noted that applicants have requested cancellation of claim 48, however, no such claim is pending in the instant application. Likewise on page 4 of the response applicants have requested cancellation of claim 20. However, claim 20 is not a pending claim before the entry of this claim.
4. New claims 18-20 have been entered.
5. 4-8 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9.
6. This application contains claims 4-8 drawn to an invention non-elected with traverse in Paper No. 9. A complete reply to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Information Disclosure Statement

7. Document number 8231598, 8193098, and 827189 listed in the IDS have been not been considered because they are not in English.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 3 and 17-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed method wherein the proliferated transformed tumor cells produced ex vivo in claim 3 or claim 17 are directly administered into a tumor of a subject to treat the tumor cells of the tumor in the subject, does not reasonably provide enablement for transplanting the

proliferated transformed tumor cells at any site in the subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Response to Arguments

Applicant's arguments filed 2-21-02 have been fully considered but they are not persuasive to obviate all the rejections. However, in view of the response of the applicants, the full lack of enablement set forth in the previous office action of 8-20-01 has been modified to a scope rejection. Applicants have argued that for practicing the claimed invention an artisan would require- tumor cells from patient, composition comprising the SEQ ID NO: 1, a method for transforming cells and proliferating the transformed cells, and a method for transplanting the transformed cells into a patient. Applicants further add that based on the disclosure of the specification and the state of the art at the time of the invention, an artisan of skill would have been able to make and use the claimed invention. In support of the arguments applicants list a review article and two patents. In response, as discussed in the previous office action, it is noted that while specific vectors, promoters, genes, and routes of administration might be or may have been effective for treatment of a specific disease providing a specific therapeutic effect, gene therapy as a broad-based art is clearly unpredictable in terms of achieving levels and duration of expression of a gene of interest which results in a therapeutic effect. Applicants, in the second paragraph on page 9 of the arguments, cite the page 11 of the specification as having description that the genomic DNA of claimed invention exhibits considerations effect in gene therapy, however, these arguments are not persuasive because the indicated parts of the specification are only speculations as to what can be done with the genomic DNA, and there is no evidence that the genomic DNA exhibited any effects as argued by the applicants. Applicants have further argued that examiner has denied the usefulness of the present invention based on the unpredictability as discussed by Anderson, Romano or Golab. Again applicants arguments are misplaced because the usefulness of the

claimed invention is not being questioned, rather the issue is whether an artisan of skill at the time of the invention, based on the teachings of the specification combined with what was known in the art, would have been able to practice the claimed method. As discussed in the previous office action of 8-29-01 neither the specification nor the art of record at the time of the invention provided sufficient guidance as to how to practice the claimed invention without undue experimentation.

It is noted that in the previous office action, as summarized below, several issues of unpredictability based on the art of record and sound scientific reasoning were raised and applicants have failed to address these issues in their arguments. For example, the specification does not provide any guidance as to what vector would have been used, how would an artisan have transplanted the cells back in the subject, at what site in the subject and whether such transplanted cells would have produced IL-18 that would have been taken up by another tumor cell in sufficient amount to treat the tumor of the subject, whether any tumor could be treated, and whether IL-18 produced by cells isolated from one type of tumor could treat another type of tumor. Above all the real issue is the production of sufficient amount of IL-18 when the cells are transplanted or reinfused in the subject. The specification does not provide any guidance and evidence whether transplanted cells in vivo would have produced IL-18 and whether there would have been any treatment of the tumor. Next the question is would IL-18 treat any tumors in view of the unpredictability of the effects of IL-18 on tumors. It is noted that the claimed method encompasses treatment of any tumor type when cells are administered or transplanted by any method or at any site. For example, it is not clear whether the method would have worked if the cells were transplanted at a site other than the tumor because IL-18 would have to be produced by the transplanted cells, transported to a tumor, taken up by the IL-18 receptors of the tumor cells and produce therapeutic effect. Again, there is no evidence or disclosure whether IL-18 would have been produced in sufficient quantity so that they could reach farther sites and treat tumors. Furthermore, there is no evidence that IL-18 had anti-tumor effects on metastasis of if a tumor cell isolated from one tumor type

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transformed with the genomic DNA encoding SEQ ID NO 1 when transplanted into a subject would have treated another type of tumor.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 3, 15, and 17-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 is indefinite because it is dependent on a cancelled claim. Therefore, it is not clear as to what is the claimed invention and therefore, claim was not considered on the merits.

Claims 3 and 17 are indefinite because it is unclear as to which tumor cells, the term "the tumor cells in the subject" refers to because after transplantation of the transformed cells, the subject would have both transformed tumor cells as well as non-transformed tumor cells. Appropriate clarification and correction is required.

12. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will

the statutory period for reply expire later than SIX MONTHS from the date of this final action.

When amending claims, applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to § 1.121(c). For instructions, Applicants are referred to <http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm>.

Applicants are also requested to submit a copy of all the pending/under consideration claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Dianiece Jacobs whose telephone number is (703) 305-3388.

Ram R. Shukla, Ph.D.


DAVE T. NGUYEN
PRIMARY EXAMINER